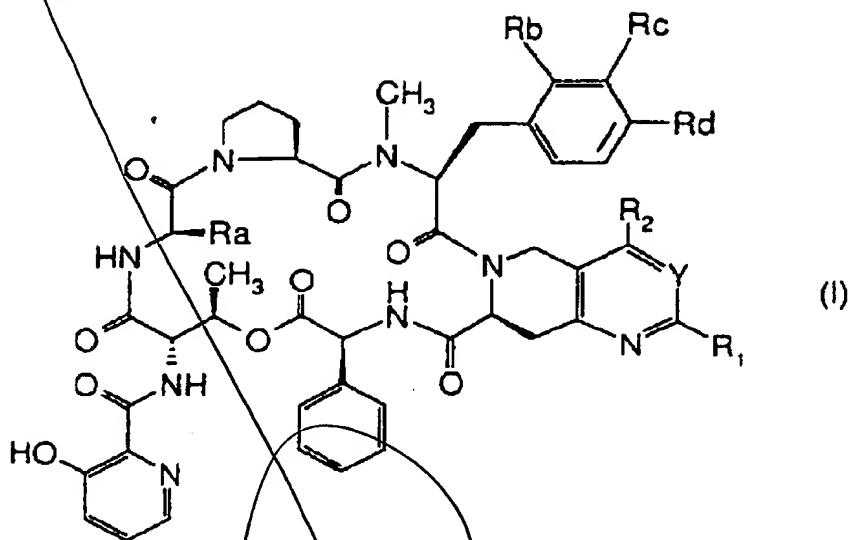


CLAIMS

What is claimed is:

- 5 1. A group B streptogramin derivative of general formula:



in which

Y is a nitrogen atom or a radical $=CR_3-$,

- 10 R_1 is a hydrogen atom, a radical alkyl (1 to 8 carbons), alkenyl (2 to 8 carbons), cycloalkyl (3 to 8 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), phenyl, phenyl which is substituted (with one or more halogen atoms or hydroxyl, alkyl, alkyloxy,
- 15 alkylthio, alkylsulphanyl, alkylsulphonyl, amino, alkylamino or dialkylamino radicals) or a radical $NR'R''$, R' and R'' , which are identical or different, being capable of being hydrogen atoms or alkyl radicals (1 to 3 carbons), or being capable of forming together
- 20 with the nitrogen atom to which they are attached a 3-

002280" 2674960

to 8-membered heterocycle optionally containing another heteroatom chosen from oxygen, sulphur or nitrogen which is optionally substituted (with a radical alkyl, alkenyl (2 to 8 carbons), cycloalkyl (3 to 6 carbons),
5 heterocyclyl which is saturated or unsaturated (4 to 6 members), benzyl, phenyl or phenyl which is substituted as defined above for the definition of R_1),
or alternatively when Y is a radical $=CR_3-$, R_1 may also be halomethyl, hydroxymethyl, alkyloxymethyl,
10 alkylthiomethyl in which the alkyl portion is optionally substituted with $NR'R''$,
alkylsulphinylmethyl, alkylsulphonylmethyl, acyloxymethyl, benzoyloxymethyl, cyclopropylaminomethyl or $-(CH_2)_nNR'R''$ (n being an integer from 1 to 4 and R'
15 and R'' being defined as above), or alternatively if R_3 is a hydrogen atom, R_1 may also be formyl, carboxyl, alkyloxycarbonyl, or $-CONR'R''$ for which R' and R'' are defined as above,
or alternatively when Y is a nitrogen atom, R_1 may also
20 be a radical $(-XR^\circ$ for which X is an oxygen or sulphur atom, a sulphinyl or sulphonyl radical, or an NH radical and R° is a radical alkyl (1 to 8 carbons), cycloalkyl (3 to 6 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members),
25 heterocyclylmethyl (3 to 8 members) in which the heterocyclyl portion is attached to the methyl radical by a carbon atom, phenyl, phenyl which is substituted (with one or more halogen atoms or hydroxyl, alkyl,

002280 2644560

alkyloxy, alkylthio, alkylsulphinyl, alkylsulphonyl,
amino, alkylamino or dialkylamino radicals) or a
radical $-(CH_2)_nNR'R''$ for which R' and R'' are defined as
above and n is an integer from 2 to 4, or alternatively
5 if X represents NH , R^o may also represent the hydrogen
atom,

R_2 is a hydrogen atom or an alkyl radical (1 to 3
carbons),

R_3 is a hydrogen atom or an alkyl, carboxyl,
10 alkyloxycarbonyl or carbamoyl radical having the
structure $-CO-NR'R''$ in which R' and R'' are defined as
above,

R_a is a methyl or ethyl radical, and

R_b , R_c and R_d have the definitions below:

- 15 1) R_b and R_c are hydrogen atoms and R_d is a hydrogen
atom or a methylamino or dimethylamino radical,
2) R_b is a hydrogen atom, R_c is a hydrogen, chlorine
or bromine atom, or represents an alkenyl radical
(3 to 5C), and R_d is a radical $-NMe-R'''$ for which
20 R''' represents a radical alkyl, hydroxyalkyl (2
to 4C), or alkenyl (2 to 8C) which is optionally
substituted with phenyl, cycloalkyl (3 to 6C)
methyl, benzyl, benzyl which is substituted (with
one or more halogen atoms or hydroxyl, alkyl,
25 alkyloxy, alkylthio, alkylsulphinyl,
alkylsulphonyl, amino, alkylamino or dialkylamino
radicals), heterocyclylmethyl or heterocyclylethyl
in which the heterocyclyl portion is saturated or

002280 064960

- unsaturated and contains 5 to 6 members and 1 or 2 heteroatoms chosen from sulphur, oxygen or nitrogen which is optionally substituted (with a radical alkyl, alkenyl (2 to 8 carbons), cycloalkyl (3 to 6 carbons), heterocyclyl which is saturated or unsaturated (4 to 6 members), phenyl, phenyl which is substituted as defined above for the definition of R_1 or benzyl), or alternatively R''' represents a radical cyanomethyl, or $-CH_2CORE$ for which either Re is $-OR'e$, $R'e$ being hydrogen, alkyl (1 to 6 carbons), alkenyl (2 to 6 carbons), benzyl or heterocyclylmethyl in which the heterocyclyl portion contains 5 to 6 members and 1 or 2 heteroatoms chosen from sulphur, oxygen or nitrogen, or Re is an alkylamino, alkylmethylamino, heterocyclylamino or heterocyclylmethylamino radical in which the heterocyclyl portion is saturated and contains 5 to 6 members and 1 or 2 heteroatoms chosen from sulphur, oxygen or nitrogen which is optionally substituted with an alkyl, benzyl or alkyloxycarbonyl radical,
- 3) R_b is a hydrogen atom, R_d is a radical $-NHCH_3$ or $-N(CH_3)_2$ and R_c is a chlorine or bromine atom, or represents an alkenyl radical (3 to 5C), (if R_d is $-N(CH_3)_2$),
- 4) R_b and R_d are hydrogen atoms and R_c is a halogen atom, or an alkylamino or dialkylamino, alkyloxy,

002280 082200 09643197

trifluoromethoxy, thioalkyl, alkyl (1 to 6C) or trihalomethyl radical,

5) Rb and Rc are hydrogen atoms and Rd is a halogen atom, or an ethylamino, diethylamino or

methylethylamino, alkyloxy or trifluoromethoxy, alkylthio, alkylsulphinyl, alkylsulphonyl, alkyl (1 to 6C), phenyl or trihalomethyl radical,

6) Rb is a hydrogen atom and Rc is a halogen atom or an alkylamino or dialkylamino, alkyloxy or

trifluoromethoxy, thioalkyl or alkyl (1 to 3C) radical, and Rd is a halogen atom or an amino, alkylamino or dialkylamino, alkyloxy or trifluoromethoxy, thioalkyl, alkyl (1 to 6C) or trihalomethyl radical,

7) Rc is a hydrogen atom and Rb and Rd represent a methyl radical,

the alkyl, alkenyl or acyl radicals being straight or branched and, unless otherwise stated, the alkyl or acyl radicals containing 1 to 4 carbon atoms, as well

as its salts when they exist.

2. A group B streptogramin derivative according to claim 1, wherein

Y is a nitrogen atom or a radical $=CR_3-$,

R₁ is a hydrogen atom, a radical alkyl (1 to 8 carbons), cycloalkyl (3 to 8 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), phenyl, phenyl which is substituted (with one or more amino,

alkylamino or dialkylamino radicals) or a radical
NR'R", R' and R", which are identical or different,
being capable of being hydrogen atoms or alkyl radicals
(1 to 3 carbons), or being capable of forming together
5 with the nitrogen atom to which they are attached a 3-
to 8-membered heterocycle optionally containing another
heteroatom chosen from oxygen, sulphur or nitrogen
which is optionally substituted with an alkyl radical,
or alternatively when Y is a radical =CR₃-, R₁ may also
10 be halomethyl, hydroxymethyl, alkylthiomethyl in which
the alkyl portion is optionally substituted with NR'R",
alkylsulphinylmethyl, alkylsulphonylmethyl,
acyloxymethyl, cyclopropylaminomethyl or -(CH₂)_nNR'R" (n
being an integer from 1 to 4 and R' and R" being
15 defined as above), or alternatively if R₃ is a hydrogen
atom, R₁ may also be formyl or -CONR'R" for which R' and
R" are defined as above,
or alternatively when Y is a nitrogen atom, R₁ may also
be a radical -XR° for which X is an oxygen or sulphur
20 atom, a sulphinyl or sulphonyl radical, or an NH
radical and R° is a radical alkyl (1 to 8 carbons),
heterocyclylmethyl (3 to 8 members) in which the
heterocyclyl portion is attached to the methyl radical
by a carbon atom, or a radical -(CH₂)_nNR'R" for which R'
25 and R" are defined as above and n is an integer from 2
to 4,
R₂ is a hydrogen atom or an alkyl radical (1 to 3
carbons),

002280" / 6 FEB 66

R₃ is a hydrogen atom or a carboxyl or alkyloxycarbonyl radical;

R_a is a methyl or ethyl radical, and

R_b, R_c and R_d have the definitions below:

- 5 • R_b and R_c are hydrogen atoms and R_d is a hydrogen atom or a methylamino or dimethylamino radical,
 • R_b is a hydrogen atom, R_d is a radical -NHCH₃ or -N(CH₃)₂ and R_c is a chlorine or bromine atom, as well as its salts when they exist.

10

3. A group B streptogramin derivative according to claim 1, wherein
Y is a nitrogen atom or a radical =CR₃-,
R₁ is a hydrogen atom, a radical alkyl (1 to 3 carbons),
15 cycloalkyl (3 to 8 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), phenyl, phenyl which is substituted with an amino radical, or alternatively when Y is a radical =CR₃-, R₁ may also be acyloxymethyl,

- 20 or alternatively when Y is a nitrogen atom, R₁ may also be a radical -XR° for which X is an oxygen or sulphur atom or a radical NH and R° is an alkyl radical (1 to 4 carbons) or a radical -(CH₂)_nNR'R" for which R' and R" which are identical or different may be hydrogen atoms
25 or alkyl radicals (1 to 3 carbons), or form together with the nitrogen atom to which they are attached a 3- to 8-membered heterocycle optionally containing another heteroatom chosen from oxygen, sulphur or nitrogen

002280" 26TE4960

optionally substituted with an alkyl radical, and n is an integer from 2 to 4,

R₂ is a hydrogen atom or an alkyl radical (1 to 3 carbons),

5 R₃ is a hydrogen atom or an alkyloxycarbonyl radical,

R_a is a methyl or ethyl radical, and

R_b, R_c and R_d have the definitions below:

• R_b and R_c are hydrogen atoms and R_d is a hydrogen atom or a methylamino or dimethylamino radical,

10 • R_b is a hydrogen atom, R_d is a radical -NHCH₃ or -N(CH₃)₂ and R_c is a chlorine atom,

as well as its salts when they exist.

4. A group B streptogramin derivative
15 according to claim 1, which is
2"-methylpyrido[2,3-5γ,5δ]pristinamycin I_E.

5. A group B streptogramin derivative
according to claim 1, which is
20 2"-cyclopropylpyrido[2,3-5γ,5δ]pristinamycin I_E.

6. A group B streptogramin derivative
according to claim 1, which is
pyrido[2,3-5γ,5δ]pristinamycin I_E.

25

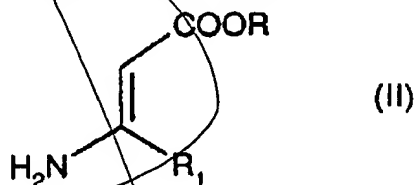
7. A group B streptogramin derivative
according to claim 1, which is

002280" 082200

2"-ethylpyrido[2,3-5 γ ,5 δ](4 ζ -methylamino)-
(4 ζ -dedimethylamino)pristinamycin I_E.

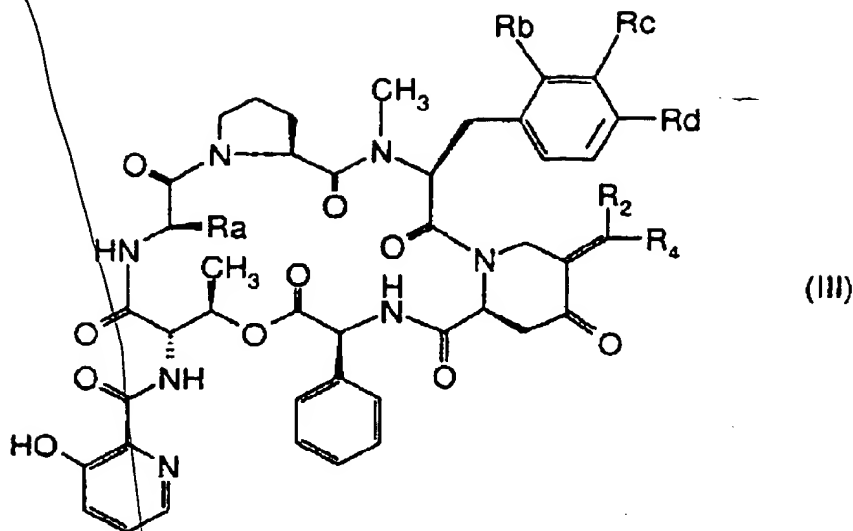
8. A group B streptogramin derivative
5 according to claim 1, which is
4 ϵ -chloro-2"-ethylpyrido[2,3-5 γ ,5 δ](4 ζ -methylamino)-
(4 ζ -dedimethylamino)pristinamycin I_E.

9. A process for the preparation of a
10 streptogramin derivative according to claim 1, wherein
Y is a radical =CR₃- and R₃ is other than an alkyl
radical, wherein an enamino ester of general formula:



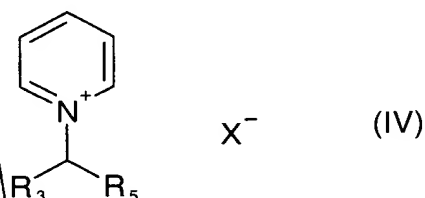
in which R₁ is defined as above and R represents the
15 residue of an easily hydrolysable ester or an alkyl
radical, is reacted with the corresponding
5 δ -methylenepristinamycin derivative of general
formula:

002280" 06T4960



in which Ra, Rb, Rc and Rd are defined as for claim 1,
 R₂ is defined as for claim 1 and R₄ is a hydrogen atom,
 or R₂ represents a hydrogen atom and R₄ is a hydrogen
 5 atom or a dialkylamino radical, followed where
 appropriate by the conversion of the ester obtained to
 an acid, and then optionally by its decarboxylation, or
 by the conversion of the acid to a carbamoyl radical
 according to the derivative according to claim 1
 10 desired, and/or followed where appropriate by the
 conversion of the derivative according to claim 1 for
 which R₁ is hydroxymethyl to a derivative for which R₁
 is a radical formyl, and then where appropriate
 carboxyl, and then where appropriate alkyloxycarbonyl
 15 or -CONR'R" and/or optionally followed by the mono-
 N-demethylation of the derivative according to claim 1
 for which Rd is a dimethylamino radical to a derivative
 for which Rd is methylamino, and then optionally
 followed by the conversion to a salt when they exist.

10. A process for the preparation of a streptogramin derivative according to claim 1, for which Y is a radical $=CR_3-$ and R_3 is a hydrogen atom or an alkyl radical, wherein a pyridinium salt of general
5 formula:



in which R_3 is defined as above, R_5 is the residue of a ketone R_1-CO- for which R_1 is defined as above with the exception of representing a radical $-NR'R''$, or
10 optionally represents a protected hydroxyl radical or a nitrophenyl radical or alternatively R_5 represents the cyano radical so as to obtain a streptogramin derivative for which R_1 is an amino radical, and X^- is an anion, is reacted with the corresponding 5 δ -
15 methylenepristinamycin derivative of general formula (III) defined in claim 2, in which R_4 is a hydrogen atom and R_a , R_b , R_c , R_d and R_2 are defined as for claim 1, optionally followed by the liberation of the hydroxyl radical or where appropriate the reduction of the
20 nitrophenyl radical so as to obtain a derivative for which R_1 is an aminophenyl radical, or optionally followed by the reaction of an amine of general formula $HNR'R''$ with the streptogramin derivative according to claim 1, for which R_1 is halomethyl, so as to obtain the
25 corresponding derivative for which R_1 is a radical $-CH_2NR'R''$, or where appropriate by the conversion of the

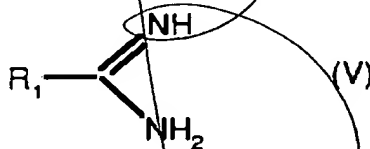
002280" J6F4960

derivative according to claim 1 for which R_1 is hydroxymethyl to a derivative for which R_1 is a radical formyl, and then where appropriate carboxyl, and then where appropriate alkylloxycarbonyl or $-\text{CONR}'\text{R}''$ and/or optionally the mono-N-demethylation of the derivative according to claim 1 for which R_d is a dimethylamino radical to a derivative for which R_d is methylamino, and then optionally followed by the conversion to a salt, when they exist.

10

11. A process for the preparation of a streptogramin derivative according to claim 1, for which Y is a nitrogen atom, wherein an amidine salt or a derivative of isourea or of isothiurea of general formula:

15



in which R_1 is defined as for claim 1, with the exception of representing a radical XR° for which X is sulphonyl or sulphinyl, or a radical $\text{NR}'\text{R}''$ other than amino, is reacted with a streptogramin derivative of general formula (III) as defined in claim 2, for which R_4 is dialkylamino, and then in order to obtain a streptogramin derivative according to claim 1, for which R_1 is a radical XR° for which X is sulphonyl or sulphinyl, the corresponding derivative for which X is a sulphur atom is oxidized, and then in order to obtain

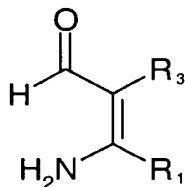
25

002280" 26 FEB 1960

the streptogramin derivative according to claim 1, for which R_1 is a radical $NR'R''$, the sulphonyl derivative obtained is substituted by the action of the corresponding amine $HNR'R''$ and/or optionally in order to obtain a derivative for which R_d is methylamino, the mono-N-demethylation of the derivative according to claim 1, for which R_d is a dimethylamino radical is carried out, and then optionally converted to a salt, when they exist.

10

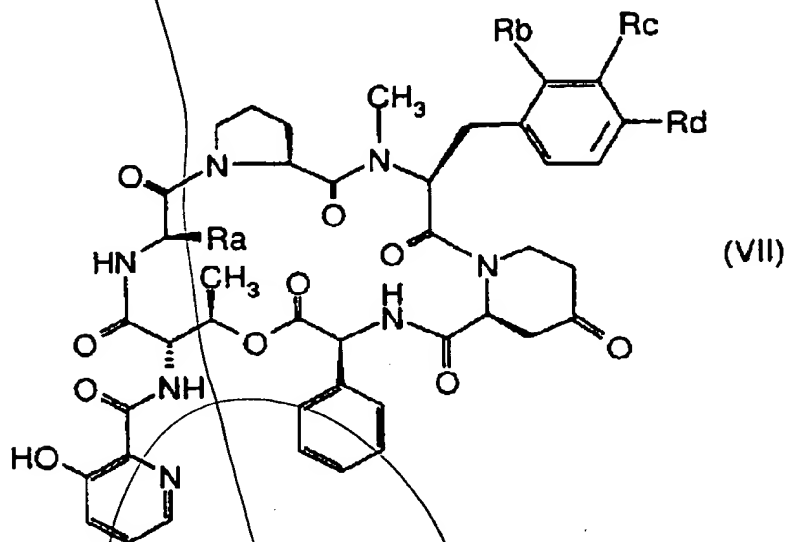
12. A process for the preparation of a streptogramin derivative according to claim 1, for which Y is a radical $=CR_3-$, R_1 is a hydrogen atom, an alkyl, alkenyl, cycloalkyl, aromatic heterocyclyl, phenyl, substituted phenyl, halomethyl, hydroxymethyl, alkyloxymethyl, alkylthiomethyl, alkylsulphinylmethyl, alkylsulphonylmethyl or $-(CH_2)_nNR'R''$ radical, or alternatively when R_3 is a hydrogen atom, for which R_1 is formyl, carboxyl, alkyloxycarbonyl or $-CONR'R''$ as defined for claim 1 and R_2 is a hydrogen atom, wherein the formyl enamine of general formula:



(VI)

in which R_1 is a hydrogen atom, an alkyl, alkenyl, cycloalkyl, aromatic heterocyclyl, phenyl, substituted phenyl, hydroxymethyl, alkyloxymethyl, alkylthiomethyl

or $-(CH_2)_nNR'R''$ radical and R_3 is defined as for claim 1, with the exception of representing carboxyl, is reacted with a streptogramin derivative of general formula:



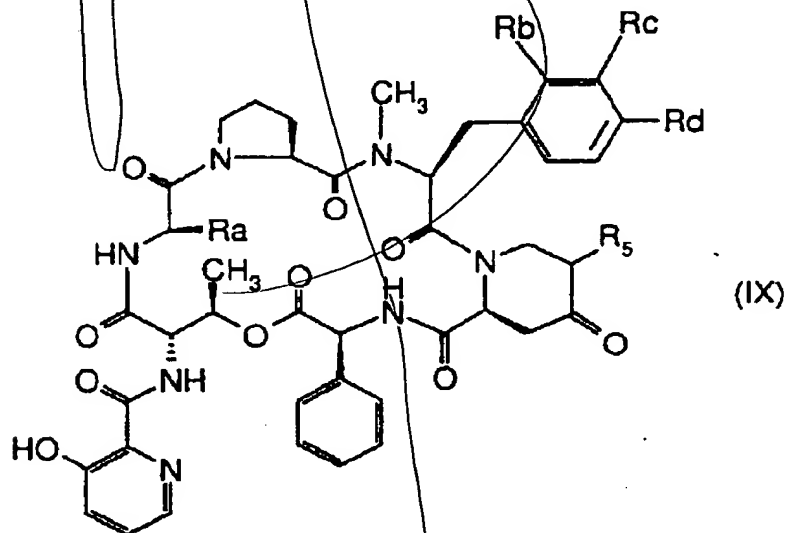
5 in which R_a , R_b , R_c and R_d are defined as for claim 1, followed where appropriate by the conversion of the derivative for which R_3 is amide or ester to a derivative for which R_3 is carboxyl and/or where
10 appropriate the oxidation of the derivative for which R_1 is alkylthiomethyl to a derivative for which R_1 is alkylsulphinylmethyl or alkylsulphonylmethyl, or where appropriate the conversion of the derivative for which R_1 is a hydroxymethyl radical to a derivative for which
15 R_1 is halomethyl, and then where appropriate the conversion of the derivative for which R_1 is halomethyl to a derivative for which R_1 is $-CH_2NR'R''$, or where appropriate the conversion of the derivative according to claim 1, for which R_1 is hydroxymethyl to a
20 derivative for which R_1 is a radical formyl, and then

where appropriate carboxyl, alkyloxycarbonyl and/or
-CONR'R", and/or optionally the mono-N-demethylation of
the derivative according to claim 1, for which Rd is a
dimethylamino radical to a derivative for which Rd is
5 methylamino, and then optionally followed by conversion
to a salt, when they exist.

13. A process for the preparation of a
streptogramin derivative according to claim 1, for
10 which Rd is methylamino, wherein the mono-N-
demethylation of the derivative according to claim 1,
for which Rd is a dimethylamino radical, is carried out
and then the streptogramin derivative obtained is
optionally converted to a salt.

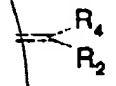
15

14. A streptogramin derivative of general
formula:



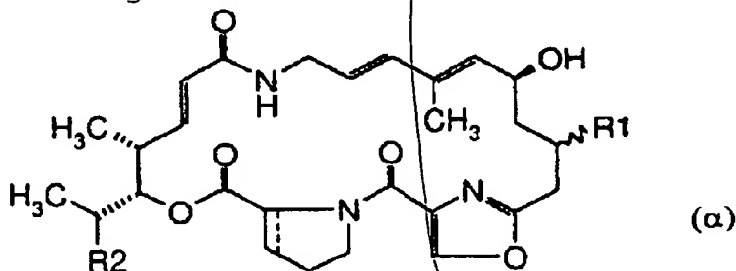
in which Ra is a methyl radical and Rb, Rc and Rd are
20 defined as in claim 1, or Ra is an ethyl radical and

Rb, Rc and Rd are defined as in claim 1 in 2) to 7) and
R₅ represents a disubstituted methylenyl radical having

the structure  for which R₂ and R₄ are defined as
above, or alternatively in which Ra, Rb, Rc and Rd are
5 defined as for claim 1 in 2), except for R''
representing ethyl if Rb and Rc are hydrogen, and R₅ is
a hydrogen atom.

15. A pharmaceutical composition comprising
10 a group B streptogramin derivative according to claim
1, in a pure state or in the form of a combination with
at least one group A streptogramin derivative, where
appropriate in the form of a salt, and/or in the form
of a combination with one or more compatible and
15 pharmaceutically acceptable diluents or adjuvants.

16. A pharmaceutical composition according
to claim 15, wherein the group A streptogramin
derivative is chosen from pristinamycin II_A,
20 pristinamycin II_B, pristinamycin II_C, pristinamycin II_D,
pristinamycin II_E, pristinamycin II_F, pristinamycin II_G
or from known semisynthetic derivatives or from the
derivatives of general formula:



in which R_1 is a radical $-NR'R''$ for which R' is a hydrogen atom or a methyl radical, R'' is a hydrogen atom, an alkyl, cycloalkyl, allyl, propargyl, benzyl or $-OR'''$, R''' radical being a hydrogen atom, an alkyl, 5 cycloalkyl, allyl, propargyl or benzyl radical, or $-NR_3R_4$, it being possible for R_3 and R_4 to represent a methyl radical, or to form together with the nitrogen atom to which they are attached a saturated or unsaturated 4- or 5-membered heterocycle which may in 10 addition contain another heteroatom chosen from nitrogen, oxygen or sulphur, R_2 is a hydrogen atom or a methyl or ethyl radical, and the bond $---$ represents a single bond or a double bond, as well as their salts.

- 15 17. A combination of a group B streptogramin derivative according to claim 1 with at least one group A streptogramin derivative as defined in claim 16.

Add
B'

002280" 2644360